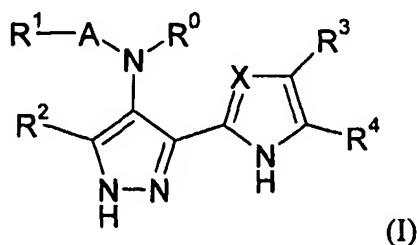


CLAIMS

1. The use of a compound for the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by a cyclin dependent kinase or glycogen synthase kinase-3 or an Aurora kinase, the compound having the formula (I):



or a salt, N-oxide or solvate thereof;

wherein

10 X is CR⁵ or N;

 A is a bond or -(CH₂)_m-(B)_n-;

 B is C=O, NR^g(C=O) or O(C=O) wherein R^g is hydrogen or C₁₋₄ hydrocarbyl optionally substituted by hydroxy or C₁₋₄ alkoxy;

 m is 0, 1 or 2;

15 n is 0 or 1;

 R⁰ is hydrogen or, together with NR^g when present, forms a group -(CH₂)_p- wherein p is 2 to 4;

 R¹ is hydrogen, a carbocyclic or heterocyclic group having from 3 to 12 ring members, or an optionally substituted C₁₋₈ hydrocarbyl group;

20 R² is hydrogen, halogen, methoxy, or a C₁₋₄ hydrocarbyl group optionally substituted by halogen, hydroxyl or methoxy;

 R³ and R⁴ together with the carbon atoms to which they are attached form an optionally substituted fused carbocyclic or heterocyclic ring having from 5 to 7 ring members of which up to 3 can be heteroatoms selected from N, O and S; and

25 R⁵ is hydrogen, a group R² or a group R¹⁰ wherein R¹⁰ is selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino,

mono- or di-C₁₋₄ hydrocarbyl amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members; a group R^a-R^b wherein R^a is a bond, O, CO, X¹C(X²), C(X²)X¹, X¹C(X²)X¹, S, SO, SO₂, NR^c, SO₂NR^c or NR^cSO₂; and R^b is selected from hydrogen, carbocyclic and heterocyclic groups having from 3 to 12 ring members, and a C₁₋₈ hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di-C₁₋₄ hydrocarbyl amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the C₁₋₈ hydrocarbyl group may optionally be replaced by O, S, SO, SO₂, NR^c, X¹C(X²), C(X²)X¹ or X¹C(X²)X¹;

R^c is selected from hydrogen and C₁₋₄ hydrocarbyl; and

X¹ is O, S or NR^c and X² is =O, =S or =NR^c.

2. The use according to claim 1 wherein the medicament is for the prophylaxis or treatment of a disease state or condition mediated by a cyclin dependent kinase or glycogen synthase kinase-3.
3. The use according to claim 1 wherein the medicament is for the prophylaxis or treatment of a disease state or condition mediated by an Aurora kinase.
- 20 4. The use according to any one of the preceding claims wherein X is N.
5. The use according to any one of the preceding claims 4 wherein m is 0 or 1 (preferably 0), n is 1 and B is C=O.
6. The use according to any one of the preceding claims wherein R⁰ is hydrogen.
- 25 7. The use according to any one of the preceding claims wherein B is NR^g(C=O) and R^g is hydrogen.

15. The use according to claim 8 wherein R¹ is a non-aromatic group selected from monocyclic cycloalkyl groups and azacycloalkyl groups such as cyclohexyl, cyclopentyl, and piperidinyl.
16. The use according to any one of claims 8 to 15 wherein the carbocyclic or heterocyclic group R¹ is an unsubstituted group.
5
17. The use according to any one of claims 8 to 15 wherein the carbocyclic or heterocyclic group R¹ bears one or more substituents selected from the group R¹⁰ as defined in claim 1.
18. The use according to claim 17 wherein the substituents on R¹ are selected from the group R^{10a} consisting of halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, heterocyclic groups having 5 or 6 ring members and up to 2 heteroatoms selected from O, N and S, a group R^a-R^b wherein R^a is a bond, O, CO, X³C(X⁴), C(X⁴)X³, X³C(X⁴)X³, S, SO, or SO₂, and R^b is selected from hydrogen, heterocyclic groups having 5 or 6 ring members and up to 2 heteroatoms selected from O, N and S, and a C₁₋₈ hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di-C₁₋₄ hydrocarbylamino, carbocyclic and heterocyclic groups having 5 or 6 ring members and up to 2 heteroatoms selected from O, N and S; wherein one or more carbon atoms of the C₁₋₈ hydrocarbyl group may optionally be replaced by O, S, SO, SO₂, X³C(X⁴), C(X⁴)X³ or X³C(X⁴)X³; X³ is O or S; and X⁴ is =O or =S.
10
15
20
19. The use according to claim 18 wherein the substituents on R¹ are selected from the group R^{10b} consisting of halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, a group R^a-R^b wherein R^a is a bond, O, CO, X³C(X⁴), C(X⁴)X³, X³C(X⁴)X³, S, SO, or SO₂, and R^b is selected from hydrogen and a C₁₋₈ hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy; wherein one or more carbon atoms of the C₁₋₈ hydrocarbyl group
25

may optionally be replaced by O, S, SO, SO₂, X³C(X⁴), C(X⁴)X³ or X³C(X⁴)X³; X³ is O or S; and X⁴ is =O or =S.

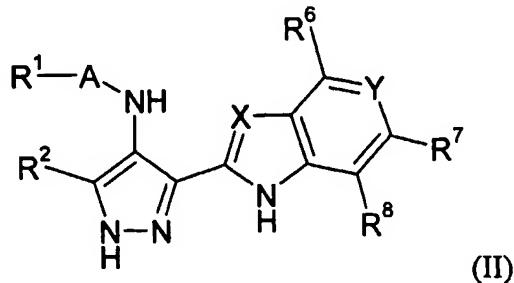
20. The use according to claim 19 wherein the substituents on R¹ are selected from halogen, hydroxy, trifluoromethyl, a group R^a-R^b wherein R^a is a bond or O, and R^b is selected from hydrogen and a C₁₋₄ hydrocarbyl group optionally substituted by one or more substituents selected from hydroxyl and halogen.

5 21. The use according to any one of claims 17 to 20 wherein R¹ is substituted by 1 or 2 or 3 or 4 substituents.

10 22. The use according to claim 21 wherein R¹ is a phenyl group which is 2,6-disubstituted, 2,3-disubstituted, 2,4-disubstituted 2,5-disubstituted, 2,3,6-trisubstituted or 2,4,6-trisubstituted.

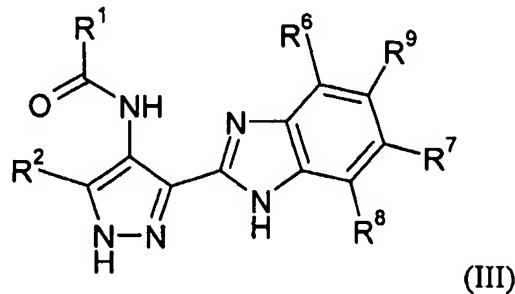
15 23. The use according to claim 22 wherein R¹ is a phenyl group which is disubstituted at positions 2- and 6- with substituents selected from fluorine, chlorine and R^a-R^b, where R^a is O and R^b is C₁₋₄ alkyl.

24. The use according to any one of the preceding claims wherein the compound is represented by the formula (II):



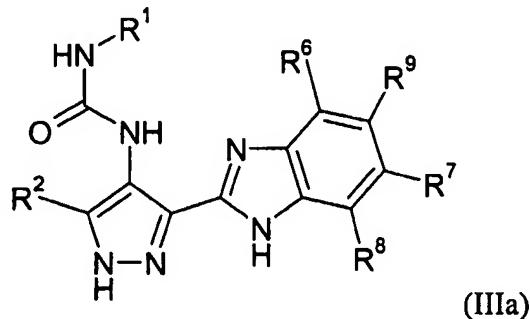
wherein R¹, R² and X are as defined in any one of the preceding claims; 20 Y is N or CR⁹ wherein R⁹ is hydrogen or a group R¹⁰; and R⁶, R⁷ and R⁸ are the same or different and each is hydrogen or a group R¹⁰ as defined in any one of the preceding claims.

25. The use according to claim 24 wherein the compound is represented by the formula (III):



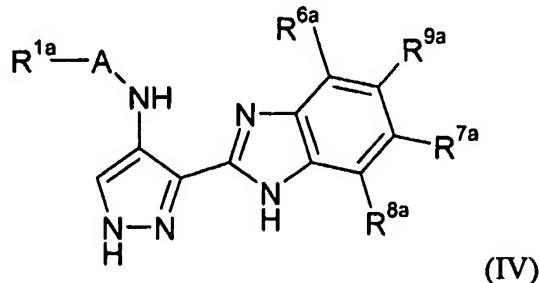
5 wherein R¹, R² and R⁶ to R⁹ are as defined in any one of the preceding claims.

26. The use according to claim 24 wherein the compound is represented by the formula (IIIa):



wherein R¹, R² and R⁶ to R⁹ are as defined in the preceding claims.

10 27. A compound of the formula (IV):



or a salt, N-oxide or solvate thereof;

wherein A is NH(C=O), O(C=O) or C=O;

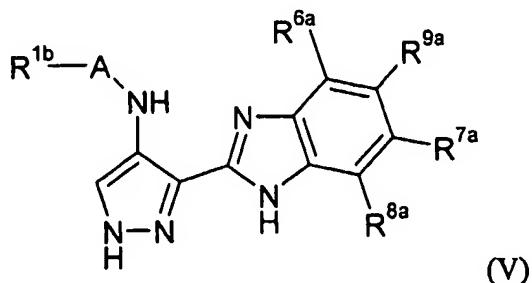
R^{6a} , R^{7a} , R^{8a} and R^{9a} are the same or different and each is selected from hydrogen, halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di- C_{1-4} hydrocarbyl amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members; a group R^a - R^b wherein R^a is a bond, O, CO, $X^1C(X^2)$, $C(X^2)X^1$, $X^1C(X^2)X^1$, S, SO, SO_2 , NR^c , SO_2NR^c or NR^cSO_2 ; and R^b is selected from hydrogen, carbocyclic and heterocyclic groups having from 3 to 12 ring members, and a C_{1-8} hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di- C_{1-4} hydrocarbyl amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the C_{1-8} hydrocarbyl group may optionally be replaced by O, S, SO, SO_2 , NR^c , $X^1C(X^2)$, $C(X^2)X^1$ or $X^1C(X^2)X^1$; or two adjacent groups R^{6a} , R^{7a} , R^{8a} or R^{9a} together with the carbon atoms to which they are attached may form a 5-membered heteroaryl ring or a 5- or 6-membered non-aromatic heterocyclic ring, wherein the said heteroaryl and heterocyclic groups contain up to 3 heteroatom ring members selected from N, O and S; R^c is selected from hydrogen and C_{1-4} hydrocarbyl; and X^1 is O, S or NR^c and X^2 is =O, =S or = NR^c ; or an adjacent pair of substituents selected from R^{6a} , R^{7a} , R^{8a} and R^{9a} together with the carbon atoms to which they are attached may form a non-aromatic five or six membered ring containing up to three heteroatoms selected from O, N and S; R^{1a} is selected from:

- 6-membered monocyclic aryl groups substituted by one to three substituents R^{10c} provided that when the aryl group is substituted by a methyl group, at least one substituent other than methyl is present;
- 6-membered monocyclic heteroaryl groups containing a single heteroatom ring member which is nitrogen, the heteroaryl groups being substituted by one to three substituents R^{10c} ;

S, the heteroaryl groups being optionally substituted with one to three substituents selected from C₁₋₄ alkyl, trifluoromethyl, fluoro and chloro;

- 5- and 6-membered non-aromatic heterocyclic groups (e.g. pyrrolidino, piperidino, piperazine, N-methylpiperazino, morpholino) containing up to 3 heteroatoms selected from N, O and S and being optionally substituted with one to three substituents selected from C₁₋₄ alkyl, trifluoromethyl, fluoro and chloro;
- cyano, nitro, amino, C₁₋₄ alkylamino, di-C₁₋₄alkylamino, C₁₋₄ acylamino, C₁₋₄ alkoxy carbonylamino;
- a group R¹⁹-S(O)_n- where n is 0, 1 or 2 and R¹⁹ is selected from amino; C₁₋₄ alkylamino; di-C₁₋₄alkylamino; C₁₋₄ hydrocarbyl; phenyl optionally substituted with one to three substituents selected from C₁₋₄ alkyl, trifluoromethyl, fluoro and chloro; and 5- and 6-membered non-aromatic heterocyclic groups containing up to 3 heteroatoms selected from N, O and S and being optionally substituted with one to three C₁₋₄ alkyl group substituents; and
- a group R²⁰-Q- where R²⁰ is phenyl optionally substituted with one to three substituents selected from C₁₋₄ alkyl, trifluoromethyl, fluoro and chloro; and Q is a linker group selected from OCH₂, CH₂O, NH, CH₂NH, NCH₂, CH₂, NHCO and CONH.

28. A compound of the formula (V):



or a salt, N-oxide or solvate thereof;

25 wherein

A is NH(C=O) or C=O;

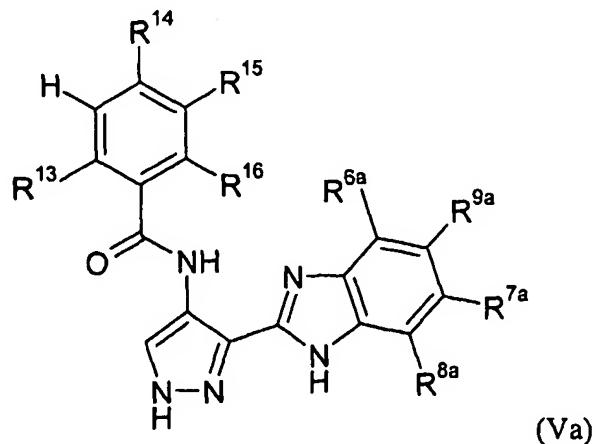
R^{1b} is a substituted phenyl group having from 1 to 4 substituents whereby:

(i) when R^{1b} bears a single substituent it is selected from halogen, hydroxyl, C_{1-4} hydrocarbyloxy optionally substituted by one or more substituents selected from hydroxyl and halogen; C_{1-4} hydrocarbyl substituted by one or more substituents selected from hydroxyl and halogen; heteroaryl groups having 5 ring members; and 5- and 6-membered non-aromatic heterocyclic groups, wherein the heteroaryl and heterocyclic groups contain up to 3 heteroatoms selected from N, O and S;

(ii) when R^{1b} bears 2, 3 or 4 substituents, each is selected from halogen, hydroxyl, C_{1-4} hydrocarbyloxy optionally substituted by one or more substituents selected from hydroxyl and halogen; C_{1-4} hydrocarbyl optionally substituted by one or more substituents selected from hydroxyl and halogen; heteroaryl groups having 5 ring members; amino; and 5- and 6-membered non-aromatic heterocyclic groups; or two adjacent substituents together with the carbon atoms to which they are attached form a 5-membered heteroaryl ring or a 5- or 6-membered non-aromatic heterocyclic ring; wherein the said heteroaryl and heterocyclic groups contain up to 3 heteroatoms selected from N, O and S; and

R^{6a} , R^{7a} , R^{8a} and R^{9a} are as defined in claim 8.

29. A compound of the formula (Va):



or a salt, N-oxide or solvate thereof;

wherein R^{6a} to R^{9a} are as defined in claim 8; and

(i) R^{13} is methoxy and R^{14} to R^{16} each are hydrogen; or

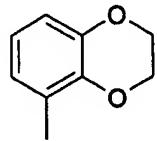
(ii) R^{14} is oxazolyl, imidazolyl or thiazolyl, preferably oxazolyl, and

5 R^{13} , R^{15} and R^{16} each are hydrogen; or

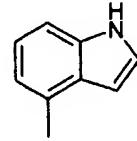
(iii) R^{13} is selected from fluorine, chlorine and methyl, R^{16} is selected from fluorine, chlorine, methyl and methoxy, and R^{14} and R^{15} each are hydrogen; or

10 (iv) R^{13} and R^{16} each are selected from fluorine, chlorine and methyl; R^{14} is selected from fluorine, chlorine, methyl and methoxy; and R^{15} is hydrogen; or

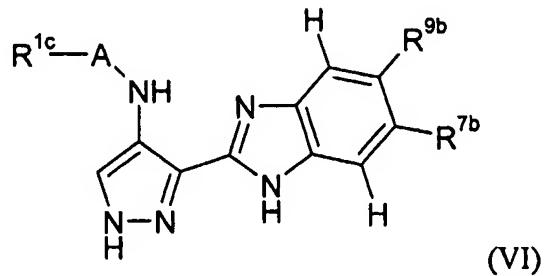
15 (v) R^{13} and R^{14} each are hydrogen; R^{15} is selected from fluorine, chlorine, methyl and methoxy (more preferably methyl and methoxy), and R^{16} is selected from fluorine, chlorine and methyl (more preferably fluorine), or R^{15} and R^{16} together with the carbon atoms of the phenyl ring form a group selected from:



and



30. A compound of the formula (VI):



20 or a salt, N-oxide or solvate thereof;

wherein:

when A is $\text{NH}(\text{C}=\text{O})$ or $\text{C}=\text{O}$;

R^{1c} is selected from:

(a) a mono-substituted phenyl group wherein the substituent is selected from *o*-amino, *o*-methoxy; *o*-chloro; *p*-chloro; *o*-difluoromethoxy; *o*-trifluoromethoxy; *o*-*tert*-butyloxy; *m*-methylsulphonyl and *p*-fluoro;

5 (b) a 2,4- or 2,6-disubstituted phenyl group wherein one substituent is selected from *o*-methoxy, *o*-ethoxy, *o*-fluoro, *p*-morpholino and the other substituent is selected from *o*-fluoro, *o*-chloro, *p*-chloro, and *p*-amino;

10 (c) a 2,5-disubstituted phenyl group wherein one substituent is selected from *o*-fluoro and *o*-methoxy and the other substituent is selected from *m*-methoxy, *m*-isopropyl; *m*-fluoro, *m*-trifluoromethoxy, *m*-trifluoromethyl, *m*-methylsulphonyl, *m*-pyrrolidinosulphonyl, *m*-(4-methylpiperazin-1-yl)sulphonyl, *m*-morpholinosulphonyl, *m*-methyl, *m*-chloro and *m*-aminosulphonyl;

15 (d) a 2,4,6-tri-substituted phenyl group where the substituents are the same or different and are each selected from *o*-methoxy, *o*-fluoro, *p*-fluoro, *p*-methoxy provided that no more than one methoxy substituent is present;

(e) a 2,4,5-tri-substituted phenyl group where the substituents are the same or different and are each selected from *o*-methoxy, *m*-chloro and *p*-amino;

20 (f) unsubstituted benzyl; 2,6-difluorobenzyl; α,α -dimethylbenzyl; 1-phenylcycloprop-1-yl; and α -*tert*-butoxycarbonylaminobenzyl;

(g) an unsubstituted 2-furyl group or a 2-furyl group bearing a single substituent selected from 4-(morpholin-4-ylmethyl), piperidinylmethyl; and optionally a further substituent selected from methyl;

25 (h) an unsubstituted pyrazolo[1,5-*a*]pyridin-3-yl group;

(i) isoxazolyl substituted by one or two C_{1-4} alkyl groups;

(j) 4,5,6,7-tetrahydro-benz[d]isoxazol-3-yl;

(k) 3-*tert*-butyl-phenyl-1*H*-pyrazol-5-yl;

(l) quioxalinyl;

(m) benz[c]isoxazol-3-yl;

(n) 2-methyl-4-trifluoromethyl-thiazol-5-yl;

30 (o) 3-phenylamino-2-pyridyl;

(p) 1-toluenesulphonylpiperidinyl;

(q) 2,4-dimethoxy-3-pyridyl; and 6-chloro-2-methoxy-4-methyl-3-pyridyl;

(r) imidazo[2,1-b]thiazol-6-yl;

(s) 5-chloro-2-methylsulphanyl-pyrimidin-4-yl;

5 (t) 3-methoxy-naphth-2-yl;

(u) 2,3-dihydro-benz[1,4]dioxin-5-yl;

(v) 2,3-dihydro-benzfuranyl group optionally substituted in the five membered ring by one or two methyl groups;

(w) 2-methyl-benzoxazol-7-yl;

10 (x) 4-aminocyclohex-1-yl;

(y) 1,2,3,4-tetrahydro-quinolin-6-yl;

(z) 2-methyl-4,5,6,7-tetrahydro-benzfuran3-yl;

(aa) 2-pyrimidinyl-1piperidin-4-yl; and 1-(5-trifluoromethyl-2-pyridyl)-piperidin-4-yl and 1-methylsulphonylpiperidin-4-yl;

15 (ab) 1-cyanocyclopropyl;

(ac) N-benzylmorpholin-2-yl;

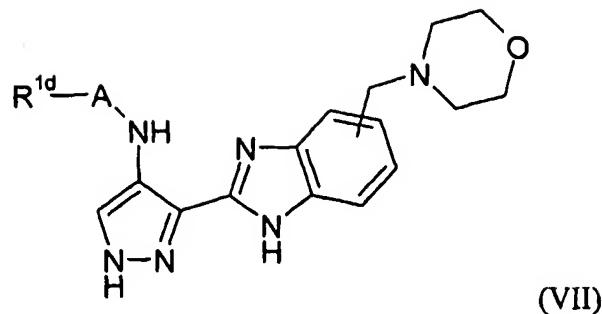
and when A is NH(C=O), R¹ is additionally selected from:

(ad) unsubstituted phenyl;

20 R^{9b} is selected from hydrogen; chlorine; methoxy; methylsulphonyl; 4-methyl-piperazin-1-ylcarbonyl; morpholinocarbonyl; morpholinomethyl; pyrrolidinylcarbonyl; N-methyl-piperidinyloxy; pyrrolidinylethoxy; morpholinopropylaminomethyl; 4-cyclopentyl-piperazin-1-ylmethyl; 4-ethylsulphonyl-piperazin-1-ylmethyl; morpholinosulphonyl; 4-(4-methylcyclohexyl)-piperazin-1-ylmethyl; and

25 R^{7b} is selected from hydrogen; methyl; methoxy and ethoxy.

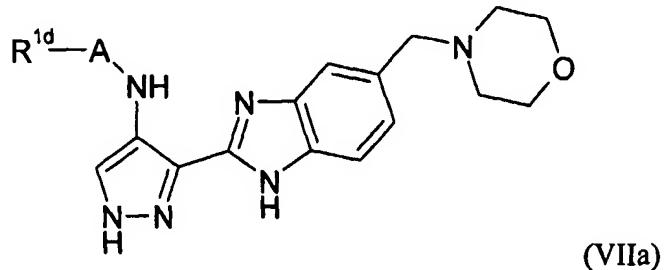
31. A compound of the formula (VII):



or a salt, N-oxide or solvate thereof;

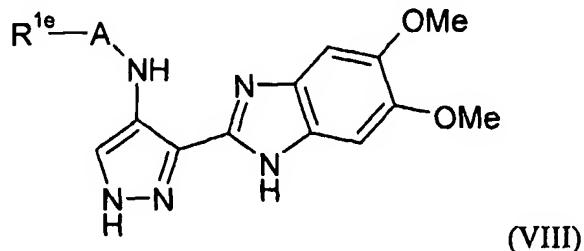
5 wherein R^{1d} is a group R^1 , R^{1a} , R^{1b} or R^{1c} as defined in any one of the preceding claims.

32. A compound according to claim 31 having the formula (VIIa):



where R^{1d} is as defined in claim 31.

33. A compound of the formula (VIII):

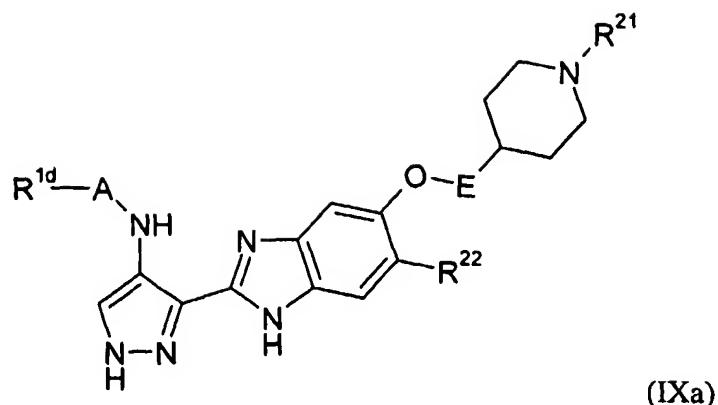


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or a salt, N-oxide or solvate thereof;

where R^{1e} is a group R^{1a} or a group R^{1b} as defined in any one of the preceding claims.

34. A compound of the formula (IX):



or a salt, N-oxide or solvate thereof;

wherein R^{1d} is as defined, E is a bond, CH_2 or CH_2CH_2 , R^{22} is selected from hydrogen, halogen (e.g. fluorine or chlorine), and C_{1-2} alkoxy (e.g. methoxy), and R^{21} is selected from hydrogen, C_{1-4} alkyl (e.g. methyl), C_{1-4} acyl, and C_{1-4} alkoxycarbonyl

35. The use of compound as defined in any one of claims 27 to 34 for the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by a cyclin dependent kinase, glycogen synthase kinase or Aurora kinase

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36. A method of inhibiting a cyclin dependent kinase, glycogen synthase kinase or Aurora kinase which method comprises contacting the kinase with a kinase-inhibiting compound of the formula (I) as defined in any one of claims 1 to 34.

15 37. A method of modulating a cellular process (for example cell division) by inhibiting the activity of a cyclin dependent kinase, glycogen synthase kinase or Aurora kinase using a compound of the formula (I) as defined in any one of claims 1 to 34.

38. A method for treating a disease or condition comprising or arising from abnormal cell growth in a mammal, which method comprises administering to the mammal a compound of formula (I) as defined in any

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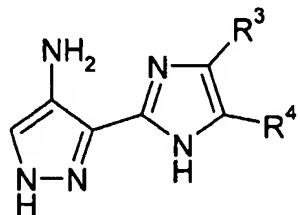
46. A use or method as defined in any one of the preceding claims wherein the disease state or condition is selected from proliferative disorders such as cancers and conditions such as viral infections, autoimmune diseases and neurodegenerative diseases.
- 5 47. A use or method according to claim 46 wherein the disease state is a cancer selected from breast cancer, ovarian cancer, colon cancer, prostate cancer, oesophageal cancer, squamous cancer, and non-small cell lung carcinomas.
- 10 48. The use of a compound as defined in any one of claims 1 to 34 for the manufacture of a medicament for the treatment or prophylaxis of a fungal infection in an animal.
- 15 49. A method for the treatment or prophylaxis of a fungal infection in an animal or plant comprising administering to the animal or plant an effective antifungal amount of a compound of the formula (I) as defined in any one of claims 1 to 34.
50. The use of a compound of the formula (I) as defined in any one of claims 1 to 34 for the manufacture of a medicament for prophylaxis or treatment of a disease or condition characterised by up-regulation of an Aurora kinase (e.g. Aurora A kinase or Aurora B kinase).
- 20 51. A method for the prophylaxis or treatment of (or alleviating or reducing the incidence of) a disease state or condition characterised by up-regulation of an Aurora kinase (e.g. Aurora A kinase or Aurora B kinase); which method comprises (i) subjecting a patient to a diagnostic test to detect a marker characteristic of up-regulation of the Aurora kinase and (ii) where the diagnostic test is indicative of up-regulation of Aurora kinase, thereafter administering to the patient a compound of the formula (I) as defined in any one of claims 1 to 34 having Aurora kinase inhibiting activity.

52. A compound as defined in any one of claims 27 to 34 for use in medicine.

53. A pharmaceutical composition comprising a compound as defined in any one of claims 27 to 34 and a pharmaceutically acceptable carrier.

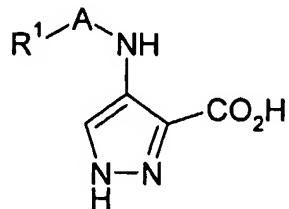
54. A process for the preparation of a compound as defined in any one of claims 1 to 34, which process comprises:

(i) the reaction of a compound of the formula:

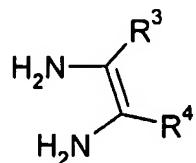


with a compound of the formula R¹-A' wherein A' is an isocyanate group N=C=O, or a group CO₂H or an activated derivative thereof; or

10 (ii) the reaction of a compound of the formula:



with a diamine compound of the formula:



wherein R¹, A, R³ and R⁴ are as defined in any one of the preceding claims; and optionally thereafter converting one compound of the formula (I) into another compound of the formula (I).